First-in-Human Investigation of the Oral First-in-Class Fatty Acid Synthase (FASN) Inhibitor, TVB-2640

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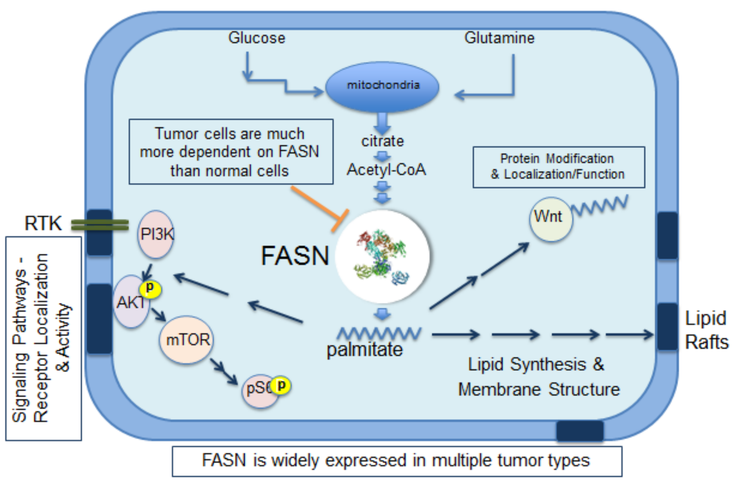
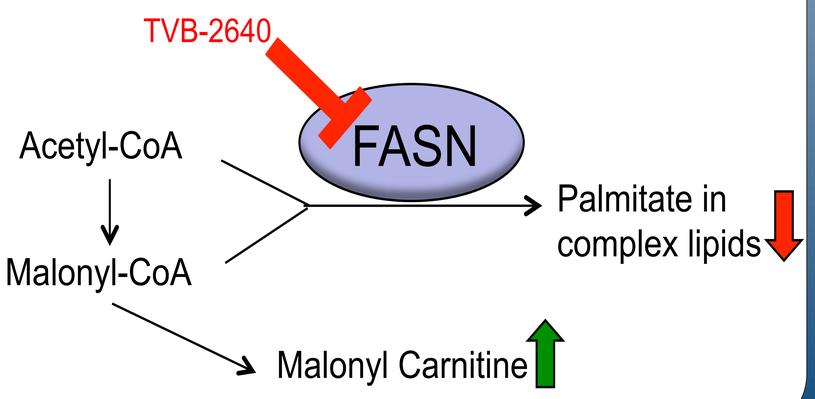
Introduction

- FASN inhibition is a novel approach to cancer treatment involving the selective disruption of palmitate biosynthesis that, in tumor cells, causes changes in cell signaling, induces apoptosis, and enhances sensitivity to other chemotherapeutic agents, in addition to other effects.
- TVB-2640 is an oral, first-in-class, small-molecule reversible inhibitor of FASN that demonstrates *in vitro* and *in vivo* anti-tumor effects with an acceptable non-clinical safety profile.
- This is a dose-escalation study in patients with metastatic or advanced-stage malignant disease refractory to standard therapy and for whom no therapy exists that would be curative or might provide significant benefit.
- Once the MTD is reached in mono- and combination- therapy, expansion cohorts in specific tumor types will be initiated.
- Preliminary data were presented at AACR 2015.

FASN-Integrated Target in Tumor Biology



Proposed Model for FASN Inhibition



Objectives

Primary: Safety, MTD, recommended phase 2 dose

Secondary: Pharmacokinetics, preliminary anti-tumor activity (monotherapy and in combination with paclitaxel)

Exploratory: Biomarkers of response and pharmacodynamic biomarkers

Study Design & Key Eligibility Criteria

- Multicenter, open label, phase 1 study
- Oral, once daily with 21 day monotherapy continuous cycles (or 28 days in combination with paclitaxel)
- Single patient, accelerated titration followed by "3+3" design after ≥ Grade 2 toxicity

Inclusion

- Adult patients with adequate bone marrow, hepatic and renal function and metastatic or advanced-stage solid malignant tumor
- Patient may have received up to 4 prior regimens of cytotoxic chemotherapy and also may have received additional prior endocrine therapy
- ECOG 0-1

Exclusion

- History of clinically significant dry eye
- Clinically significant ophthalmologic findings
- History of risk factors for torsade de pointes (e.g., heart failure, hypokalemia)
- Conditions that might interfere with oral absorption

Biomarker Tissue Requirements

Study Requirements:
- Archival and/or paired fresh biopsy
- Mandated in certain tumor types; CRC

What are we using it for:
- Genotyping
- Immunohistochemistry
- Gene expression
- Serum proteomics
- Serum metabolomics

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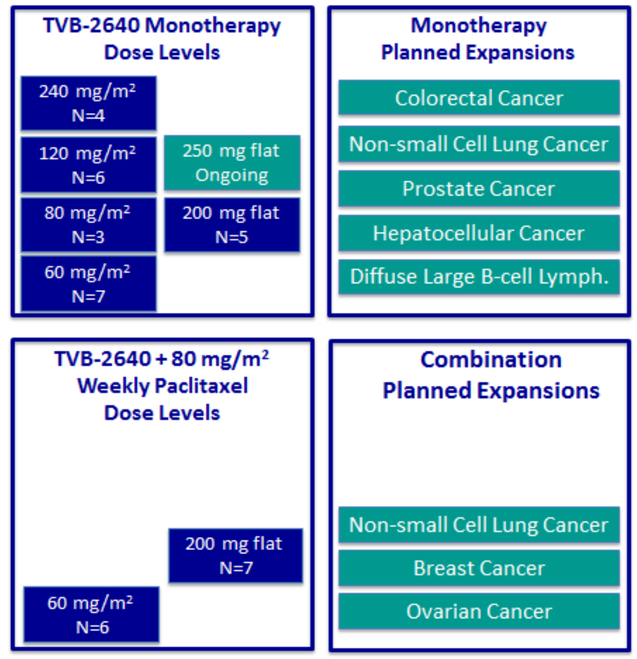
Dose Escalation and Expansion Schema



Note: Patients are being enrolled in the US and UK

Next Steps

- Multiple expansion cohorts with TVB-2640 in monotherapy and in combination with weekly paclitaxel are being initiated:
  - Monotherapy: CRC, NSCLC, Prostate, HCC, DLBCL
  - Combination Therapy: NSCLC, Breast, Ovarian

More Information

- Quick reference codes below: Data presented at AACR 2015
  - Patel et al. First-In-Human Study of the First-In-Class Fatty Acid Synthase (FASN) Inhibitor, TVB-2640
  - O'Farrell et al. Biomarker and PK/PD analysis of first in class FASN inhibitor TVB-2640 in a first-in-human phase 1 study in solid tumor patients

Thank You to the Patients and Their Families